Welcome to DIALOG

Dialog level 05.12.03D
? b 411;set files biotech
26jun06 09:08:04 User219511 Session D648.2
$0.00 0.100 DialUnits File410
$0.00 Estimated cost File410
$0.05 TELNET
$0.05 Estimated cost this search
$0.46 Estimated total session cost 0.216 DialUnits
File 411:DIALINDEX(R)

DIALINDEX(R)
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*** DIALINDEX search results display in an abbreviated ***
*** format unless you enter the SET DETAIL ON command. ***
You have 25 files in your file list.
(To see banners, use SHOW FILES command)
? s (morphogen? or osteogen?) and (protein? or polypeptide?) and (cysteine? or cystine?) and skeleton?

Your SELECT statement is:
s (morphogen? or osteogen?) and (protein? or polypeptide?) and (cysteine? or cystine?) and skeleton?

Items	File
7	5: Biosis Previews(R)_1969-2006/Jun W3
7	24: CSA Life Sciences Abstracts_1966-2006/May
9	34: SciSearch(R) Cited Ref Sci_1990-2006/Jun W3
6	71: ELSEVIER BIOBASE_1994-2006/Jun W4
7	73: EMBASE_1974-2006/Jun 26
3	94: JICST-EPlus_1985-2006/Mar W4
1	144: Pascal_1973-2006/Jun W1
10	155: MEDLINE(R)_1951-2006/Jun 20
6	357: Derwent Biotech Res._1982-2006/Jun W3
1	369: New Scientist_1994-2006/Jun W3
1	370: Science_1996-1999/Jul W3
1	399: CA SEARCH(R)_1967-2006/UD=14426

12 files have one or more items; file list includes 25 files.

? save temp; b 155,5,71,73,357;exs;rd
Temp SearchSave "TE26367867" stored
26jun06 09:10:31 User219511 Session D648.3
$3.95 1.492 DialUnits File411
$3.95 Estimated cost File411
$0.80 TELNET
$4.75 Estimated cost this search
$5.21 Estimated total session cost 1.708 DialUnits

SYSTEM:OS - DIALOG OneSearch
File 155:MEDLINE(R) 1951-2006/Jun 20
(c) format only 2006 Dialog
*File 155: Please see HELP NEWS 154
for information about recent updates added to MEDLINE.
File 5:Biosis Previews(R) 1969-2006/Jun W3
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File 71:ELSEVIER BIOBASE 1994-2006/Jun W4
(c) 2006 Elsevier Science B.V.
File 73:EMBASE 1974-2006/Jun 26
(c) 2006 Elsevier Science B.V.
File 357:Derwent Biotech Res. _1982-2006/Jun W3
(c) 2006 The Thomson Corp.

Set	Items	Description

Executing TE26367867
HILIGHT set on as '%'

Processing
136229 MORPHOGEN?
47151 OSTEOGEN?
6352830 PROTEIN?
340981 POLYPEPTIDE?
212405 CYSTEINE?
25265 CYSTINE?
80905 SKELETON?
S1 36 (MORPHOGEN? OR OSTEOGEN?) AND (PROTEIN? OR POLYPEPTIDE?) AND (CYSTEINE? OR CYSTINE?) AND SKELETON?
S2 20 RD (unique items)
? t s2/7/1-20

2/7/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

13061271 PMID: 11118896
Neuralin-1 is a novel Chordin-related molecule expressed in the mouse [illegible]
Coffinier C; Tran U; Larrain J; De Robertis E M
Howard Hughes Medical Institute, University of California, Los Angeles, CA 90095-1662, USA.
Mechanisms of development (IRELAND) Jan 2001, 100 (1) p119-22, ISSN 0925-4773--Print Journal Code: 9101218
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
%Cysteine%-rich repeats (CRs) of the type described in Chordin constitute conserved domains present in an expanding family of secreted molecules. These motifs were shown to mediate directly the antagonism of BMP signaling by Chordin and play a major role during development. Here we report the cloning and expression pattern of neuralin-1, a new member of the chordin family. The mouse cDNA was cloned by homology with a human genomic sequence encoding putative CRs. In the human genome, neuralin-1 transcripts are encoded by 8 exons that span a region of at least 80 kilobases located on chromosome Xq22.1-23. Neuralin-1 is a 333 amino acid %protein% containing three CRs, two of them highly similar to the Chordin CRs that bind BMP. Like chordin, neuralin-1 is able to induce secondary axes after mRNA injection in Xenopus embryos. Interestingly, during late gastrulation, neuralin-1 and chordin present distinct and complementary expression patterns in the mouse: neuralin-1 expression starts in the neural plate at mid-gastrulation, whereas chordin expression at that stage is restricted to the node and midline mesendoderm. Later on, neuralin-1 expression becomes restricted to discrete regions of the central nervous system and to derivatives of the neural crest cells. During organogenesis, neuralin-1 presents a broad expression pattern in many tissues such as dorsal root ganglia, gut, condensing cartilages of the %skeleton% and developing hair follicles.
Record Date Created: 20010129
Record Date Completed: 20010308

2/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

12666793 PMID: 10749571
Osteopenia and decreased bone formation in osteonectin-deficient mice.
Delany A M; Amling M; Priemel M; Howe C; Baron R; Canalis E
Department of Research, Saint Francis Hospital and Medical Center, Hartford, Connecticut 06105, USA.
Journal of clinical investigation (UNITED STATES) Apr 2000, 105 (7) p915-23, ISSN 0021-9738--Print Journal Code: 7802877
Contract/Grant No.: AR21707; AR; NIAMS; AR44877; AR; NIAMS; DE04724; DE; NIDCR
Publishing Model Print; Erratum in J Clin Invest 2000 May;105(9) 1325
Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

Bone continuously remodels in response to mechanical and physiological stresses, allowing vertebrates to renew bone as adults. Bone remodeling consists of the cycled synthesis and resorption of collagenous and noncollagenous extracellular matrix %proteins%, and an imbalance in this process can lead to disease states such as osteoporosis, or more rarely, osteopetrosis. There is evidence that the extracellular matrix glycoprotein osteonectin or secreted %protein% acidic and rich in %cysteine% (BM-40) may be important in bone remodeling. Osteonectin is abundant in bone and is expressed in areas of active remodeling outside the %skeleton%. In vitro studies indicate that osteonectin can bind collagen and regulate angiogenesis, metalloproteinase expression, cell proliferation, and cell-matrix interactions. In some osteopenic states, such as %osteogenesis% imperfecta and selected animal models for bone fragility, osteonectin expression is decreased. To determine the function of osteonectin in bone, we used contact x-ray, histomorphometry, and Northern blot analysis to characterize the skeletal phenotype of osteonectin-null mice. We found that osteonectin-null mice have decreased bone formation and decreased osteoblast and osteoclast surface and number, leading to decreased bone remodeling with a negative bone balance and causing profound osteopenia. These data indicate that osteonectin supports bone remodeling and the maintenance of bone mass in vertebrates.

Record Date Created: 20000522
Record Date Completed: 20000522

2/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12508918 PMID: 10452857

The mouse Cer1 (Cerberus related or homologue) gene is not required for anterior pattern formation.

Simpson E H; Johnson D K; Hunsicker P; Suffolk R; Jordan S A; Jackson I J
MRC Human Genetics Unit, Western General Hospital, Crewe Road, Edinburgh, EH4 2XU, United Kingdom.

Developmental biology (UNITED STATES) Sep 1 1999, 213 (1) p202-6, ISSN 0012-1606--Print Journal Code: 0372762
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

Cer1 is the mouse homologue of the Xenopus Cerberus gene whose product is able to induce development of head structures during embryonic development. The Cer1 %protein% is a member of the %cysteine% knot superfamily and is expressed in anterior regions of the mouse gastrula. A segmental pattern of expression with nascent and newly formed somites is also seen. This suggests an additional role in development of the axial %skeleton%, musculature, or peripheral nervous system. Xenopus animal cap assays and mouse germ-layer explant recombination experiments indicate that the mouse %protein% can act as a patterning molecule for anterior development in Xenopus, including induction of Otx2 expression, and suggest it may have a similar role in mouse development. However, we present here genetic data that demonstrate that Cer1 is not necessary for anterior patterning, Otx2 expression, somite formation, or even normal mouse %morphogenesis%.

Record Date Created: 19990922
Record Date Completed: 19990922

2/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11774479 PMID: 9593718

Cloning and characterization of a novel member of the transforming growth factor-beta/bone %morphogenetic% %protein% family.

Paralkar V M; Vail A L; Grasser W A; Brown T A; Xu H; Vukicevic S; Ke H Z ; Qi H; Owen T A; Thompson D D
Department of Metabolic Diseases, Central Research Division, Pfizer, Inc., Groton, Connecticut 06340, USA. Vishwas M Paralkar@groton.pfizer.com

Journal of biological chemistry (UNITED STATES) May 29 1998, 273 (22) p13760-7, ISSN 0021-9258--Print Journal Code: 2985121R
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

Members of the transforming growth factor-beta (TGF-beta) superfamily of growth and differentiation factors have been identified in a wide variety of organisms, ranging from invertebrates to mammals. Bone %morphogenetic% %proteins% (BMPs) constitute a subgroup of %proteins% belonging to the TGF-beta superfamily. BMPs were initially identified by their ability to induce endochondral bone formation at ectopic sites, suggesting a critical role for this family in development and regeneration of the %skeleton%. They are also expressed at a variety of nonskeletal sites during development, suggesting possible extraskeletal roles for these %proteins%. We cloned a novel member of the BMP family that is expressed at high levels in the placenta and the prostate and that we have designated as prostate-derived factor (PDF). Based on cDNA sequence analysis, the predicted PDF %protein% contains two %cysteines% in addition to the seven conserved %cysteines% that are the hallmark of the members of the TGF-beta superfamily. In addition, Northern blot hybridization to poly(A)+ RNA showed low levels of expression in the kidney and pancreas. We further characterized the expression of this member of the BMP family by in situ hybridization and immunohistochemistry. These results show high expression in the terminal villae of the placenta. The expression of the %protein% as visualized by immunohistochemistry shows an expression pattern identical to that of the message in the terminal villae of the placenta. In day 18 rat embryos, %protein% expression was also seen in the skin and in the cartilaginous tissue of developing %skeleton% . Orchidectomy and dihydrotestosterone treatment of rats revealed that PDF expression is regulated by androgens in the prostate. In addition, subcutaneous implantation of recombinant PDF induced cartilage formation and the early stages of endochondral bone formation. These data indicate that PDF has a functional relationship to the BMPs.

Record Date Created: 19980701
Record Date Completed: 19980701

2/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11598042 PMID: 9451821

Cartilage-derived %morphogenetic% %protein%-1.

Luyten F P
Craniofacial and Skeletal Diseases Branch, National Institute of Dental Research, National Institutes of Health, Bethesda, MD 20892-1188, USA.

international journal of biochemistry & cell biology (ENGLAND) Nov 1997 , 29 (11) p1241-4, ISSN 1357-2725--Print Journal Code: 9508482
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

A new %morphogenic% secreted %protein% has been identified with direct evidence for its involvement in skeletal development and joint %morphogenesis%. Cartilage-derived %morphogenetic% %protein%-1 (Cdmp1) and its mouse homologue growth/differentiation factor 5 (Gdf5) were discovered independently using a degenerate PCR screen for bone %morphogenetic% %protein% -like genes. Cdmp1/Gdf5 belongs to the TGF-beta superfamily, a large group of signaling molecules that are secreted as biologically active dimers with a carboxyl-terminal domain containing seven highly conserved %cysteines% . Its temporal and spatial expression pattern is mostly restricted to the developing appendicular %skeleton% . Genetic studies revealed that effective null mutations in the gene are associated with

short limbs, brachypodism (bp) in mice and acromesomelic chondrodysplasia in humans. Recombinantly expressed %protein% initiates and promotes chondrogenesis and to a limited extent %osteogenesis% in vitro and in vivo. This makes this %polypeptide% a potential therapeutic agent in the regeneration of skeletal tissues. (11 Refs.)
Record Date Created: 19980224
Record Date Completed: 19980224

2/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11592472 PMID: 9441684
Cyr61, product of a growth factor-inducible immediate-early gene, regulates chondrogenesis in mouse limb bud mesenchymal cells.
Wong M; Kireeva M L; Kolesnikova T V; Lau L F
Department of Molecular Genetics, University of Illinois College of Medicine, Chicago 60607-7170, USA.
Developmental biology (UNITED STATES) Dec 15 1997, 192 (2) p492-508, ISSN 0012-1606--Print Journal Code: 0372762
Contract/Grant No.: CA46565; CA; NCI
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Chondrogenesis during embryonic skeletal development involves the condensation of mesenchymal cells followed by their differentiation into chondrocytes. We describe herein a previously unrecognized regulator of mammalian chondrogenesis encoded by a murine growth factor-inducible immediate-early gene, cyr61. The Cyr61 %protein% is a secreted, heparin-binding %protein% (379 amino acids with 38 conserved %cysteines%) that promotes cell adhesion, migration, and proliferation. The expression pattern of the cyr61 gene during embryogenesis is tissue specific and temporally regulated. Most notably, cyr61 is transiently expressed in mesenchymal cells of both mesodermal and neuroectodermal origins undergoing chondrogenesis, suggesting that Cyr61 may play a role in the development of the embryonic %skeleton% . In this communication, we demonstrate that the Cyr61 %protein% promotes chondrogenesis in micromass cultures of limb bud mesenchymal cells in vitro and is likely to play a similar role in vivo based on the following observations: (1) Cyr61 is present in the embryonic limb mesenchyme during chondrogenesis in vivo and in vitro; (2) purified recombinant Cyr61 %protein% added exogenously to micromass cultures promotes chondrogenesis as judged by precocious expression of type II collagen, increased [35S]sulfate incorporation, and larger Alcian blue-staining cartilage nodules; (3) Cyr61 enhances cell-cell aggregation, an initial step in chondrogenesis, and promotes chondrogenic differentiation in cultures plated at subthreshold cell densities that are otherwise unable to support differentiation; and (4) neutralization of the endogenous Cyr61 with specific antibodies inhibits chondrogenesis. Taken together, these results identify Cyr61 as a novel player in chondrogenesis that contributes to the development of the mammalian embryonic %skeleton.%
Record Date Created: 19980213
Record Date Completed: 19980213

2/7/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10520689 PMID: 7615546
Isoform cloning, actin binding, and chromosomal localization of human erythroid dematin, a member of the villin superfamily.
Azim A C; Knoll J H; Beggs A H; Chishti A H
Department of Biomedical Research, St. Elizabeth's Medical Center, Tufts University School of Medicine, Boston, Massachusetts 02135, USA.
Journal of biological chemistry (UNITED STATES) Jul 21 1995, 270 (29) p17407-13, ISSN 0021-9258--Print Journal Code: 2985121R
Contract/Grant No.: HD18568; HD; NICHD; HL37462; HL; NHLBI; HL51445; HL; NHLBI
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Dematin is an actin-bundling %protein% of the erythroid membrane %skeleton% and is abundantly expressed in human brain, heart, skeletal, muscle, kidney, and lung. The 48-kDa subunit of dematin contains a headpiece domain which was originally identified in villin, and actin-binding %protein% of the brush-border cytoskeleton. The head-piece domain of villin is essential for its %morphogenic% function in vivo. Here we report the primary structure of 52-kDa subunit of dematin which differs from the 48-kDa subunit by a 22-amino-acid insertion within its headpiece domain. A unique feature of the insertion sequence of the 52-kDa subunit is its homology to erythrocyte %protein% 4.2. The insertion sequence also includes a %cysteine% residue which may explain the formation of sulfhydryl-linked trimers of dematin. Actin binding measurements using recombinant fusion %proteins% revealed that each monomer of dematin contains two F-actin binding sites: one in the headpiece domain and the other in the undefined N-terminal domain. Although the actin bundling activity of intact dematin was abolished by phosphorylation, no effect of phosphorylation was observed on the actin binding activity of fusion %proteins% . Using somatic cell hybrid panels and fluorescence in situ hybridization, the dematin gene was localized on the short arm of chromosome 8. The dematin locus, 8p21.1, is distal to the known locus of human erythroid ankyrin (8p11.2) and may contribute to the etiology of hemolytic anemia in a subset of patients with severe hereditary spherocytosis.
Record Date Created: 19950822
Record Date Completed: 19950822

2/7/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09399634 PMID: 1419914
Expression of the growth factor-inducible immediate early gene cyr61 correlates with chondrogenesis during mouse embryonic development.
O'Brien T P; Lau L F
Department of Genetics, University of Illinois College of Medicine, Chicago 60612.
Cell growth & differentiation - the molecular biology journal of the American Association for Cancer Research (UNITED STATES) Sep 1992, 3 (9) p645-54, ISSN 1044-9523--Print Journal Code: 9100024
Contract/Grant No.: CA46565; CA; NCI
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
cyr61 is a growth factor-inducible immediate early gene initially identified in serum-stimulated mouse fibroblasts. It encodes a member of an emerging family of %cysteine%-rich secreted %proteins% that includes a connective tissue growth factor. We show here that cyr61 is expressed in the developing mouse embryo and extraembryonic tissues. In the placenta, cyr61 is expressed in regions of trophoblastic origin, including the ectoplacental cone and the trophoblastic giant cells. In the midgestation embryo, cyr61 is expressed in the smooth muscle vessel walls of the arterial circulatory system. Most notably, expression is found in developing cartilaginous elements, including the limbs, ribs, and prevertebrae. In addition, regions of the chondrocranium and craniofacial elements, such as Meckel's cartilage, also express cyr61. Thus, cyr61 transcript is found in mesenchymal cells of both mesodermal and ectodermal origin during their differentiation into chondrocytes. The temporal and spatial regulation of cyr61 expression and the biochemical features of its encoded %protein% suggest that cyr61 may be important for the normal growth, differentiation, or %morphogenesis% of the cartilaginous %skeleton% of the embryo.

Record Date Created: 19921217
Record Date Completed: 19921217

2/7/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

09366640 PMID: 1393779
Alkaline phosphatase and peptidase levels in invertebrate cartilage.
Libbin R M; Hirschman A; Person P; Blumenthal N C
Department of Veterans Affairs Medical Center, Brooklyn, New York 11209.
Calcified tissue international (UNITED STATES) Jul 1992, 51 (1) p62-6, ISSN 0171-967X--Print Journal Code: 7905481
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Cartilage is encountered in the %skeletons% of many advanced invertebrates, yet it never calcifies or is replaced by bone. In an attempt to account for the absence of bone in invertebrates, we tested a hypothesis proposing that absence or inadequate quantities of several enzymes associated with vertebrate %osteogenesis% may underlie the failure of the invertebrates to evolve bone. The enzymes examined were alkaline phosphatase, alanyl beta-naphthylamidase, and neutral protease. Their activities were measured in the gill cartilage of the Atlantic horseshoe crab, Limulus polyphemus, and the odontophore cartilage of the marine whelk, Busycon canaliculatum. Animals were collected from the Cape Cod area. Samples of cartilage of Limulus perichondrium, various non-skeletal tissues, and neonatal rat calvaria, the latter as a reference standard, were homogenized in 0.1 M phosphate buffer (pH 7.1) and analyzed for %protein% content and the above-mentioned enzyme activities. Alkaline phosphatase specific activity was readily detected in most tissues except the invertebrate cartilage specimens in which it was present only at near-trace levels. Naphthylamidase and protease activities were present in all tissues. In a single experiment, higher phosphatase values were recorded for Limulus cartilage retaining perichondrium, but in a subsequent trial assaying cartilage retaining perichondrium, denuded cartilage, and isolated perichondrium separately, it was demonstrated that phosphatase activity resided primarily within the perichondrium. Exposure of thick cryostat sections to p-nitrophenyl phosphate confirmed the suspicion that alkaline phosphatase activity was present principally in the perichondrium.(ABSTRACT TRUNCATED AT 250 WORDS)
Record Date Created: 19921110
Record Date Completed: 19921110

2/7/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

09300984 PMID: 1637554
The bone %morphogenetic% %protein% family and %osteogenesis.%
Wozney J M
Genetics Institute, Inc., Cambridge, MA 02140.
Molecular reproduction and development (UNITED STATES) Jun 1992, 32 (2) p160-7, ISSN 1040-452X--Print Journal Code: 8903333
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
The BMPs (bone %morphogenetic% %proteins%) are a group of related %proteins% originally identified by their presence in bone-inductive extracts of demineralized bone. By molecular cloning, at least six related members of this family have been identified and are called BMP-2 through BMP-7. These molecules are part of the TGF-beta superfamily, based on primary amino acid sequence homology, including the absolute conservation of seven %cysteine% residues between the TGF-betas and the BMPs. The BMPs can be divided into subgroups with BMP-2 and BMP-4 being 92% identical, and BMP-5, BMP-6, and BMP-7 being an average of about 90% identical. To examine the individual activities of these molecules, we are producing each BMP in a mammalian expression system. In this system, each BMP is synthesized as a precursor peptide, which is glycosylated, processed to the mature peptide, and secreted as a homodimer. These reagents have been used to demonstrate that single molecules, such as BMP-2, are capable of inducing the formation of new cartilage and bone when implanted ectopically in a rodent assay system. Whether each of the BMPs possesses the same inductive activities in an animal is the subject of ongoing research. Based on the chondrogenic and %osteogenic% abilities of the BMPs in the adult animal, the expression of the mRNAs for the BMPs has been examined in the development of the embryonic %skeleton% by in situ hybridization. These studies demonstrate that the BMP mRNAs are spatially and temporally expressed appropriately for the %proteins% involved in the induction and development of cartilage and bone in the embryonic limb bud.(ABSTRACT TRUNCATED AT 250 WORDS) (27 Refs.)
Record Date Created: 19920901
Record Date Completed: 19920901

2/7/11 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 The Thomson Corporation. All rts. reserv.

0015956588 BIOSIS NO.: 200600301983
Role of Wnts in prostate cancer bone metastases
AUTHOR: Hall Christopher L; Kang Sona; MacDougald Ormond A; Keller Evan T (Reprint)
AUTHOR ADDRESS: RM 5304 CCGCB,1300 E Med Ctr Dr, Ann Arbor, MI 48109 USA** USA
AUTHOR E-MAIL ADDRESS: etkeller@umich.edu
JOURNAL: Journal of Cellular Biochemistry 97 (4): p661-672 MAR 1 2006 2006
ISSN: 0730-2312
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Prostate cancer (CaP) is unique among all cancers in that when it metastasizes to bone, it typically forms osteoblastic lesions (characterized by increased bone production). CaP cells produce many factors, including Wnts that are implicated in tumor-induced osteoblastic activity. In this prospectus, we describe our research on Wnt and the CaP bone phenotype. Wnts are %cysteine%-rich glycoproteins that mediate bone development in the embryo and promote bone production in the adult. Wnts have been shown to have autocrine tumor effects, such as enhancing proliferation and protecting against apoptosis. In addition, we have recently identified that CaP-produced Wnts act in a paracrine fashion to induce osteoblastic activity in CaP bone metastases. In addition to Wnts, CaP cells express the soluble Wnt inhibitor dickkopf-1 (DKK-1). If appears that DKK-1 production Occurs early in the development of skeletal metastases, which results in masking of %osteogenic% Wnts, thus favoring osteolysis at the metastatic site. As metastases progress, DKK-1 expression decreases allowing for unmasking of Wnt's osteoblastic activity and ultimately resulting in osteosclerosis at the metastatic site. We believe that DKK-1 is one of the switches that transitions the CaP bone metastasis activity from osteolytic to osteoblastic. Wnt/DKK-1 activity fits a model of CaP-induced bone remodeling occurring in, a continuum composed of an osteolytic phase, mediated by receptor activator of NFkB ligand (RANKL), parathyroid hormone-related %protein% (PTHRP) and DKK-1; a transitional phase, where environmental alterations promote expression of osteoblastic factors (Wnts) and decreases osteolytic factors (i.e., DKK-1); and an osteoblastic phase, in which tumor growth-associated hypoxia results in production of vascular endothelial growth factor and endothelin-1, which have osteoblastic activity. This model suggests that targeting both osteolytic activity and osteoblastic activity will provide efficacy for therapy of CaP bone metastases.

2/7/12 (Item 1 from file: 71)

DIALOG(R)File 71:ELSEVIER BIOBASE

01676873 2001049842
The dystrophin/utrophin homologues in Drosophila and in sea urchin
Neuman S.; Kaban A.; Volk T.; Yaffe D.; Nudel U.
ADDRESS: U. Nudel, Department of Molecular Cell Biology, Weizmann Institute of Science, Rehovot 76100, Israel
EMAIL: uri.nudel@weizmann.ac.il
Journal: Gene, 263/1-2 (17-29), 2001, Netherlands
PUBLICATION DATE: January 24, 2001
CODEN: GENED
ISSN: 0378-1119
PUBLISHER ITEM IDENTIFIER: S0378111900005849
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 50

The gene which is defective in Duchenne muscular dystrophy (DMD) is the largest known gene containing at least 79 introns, some of which are extremely large. The product of the gene in muscle, dystrophin, is a 427 kDa %protein%. The same gene encodes at least two additional non-muscle full length dystrophin isoforms transcribed from different promoters located in the 5prime-end region of the gene, and four smaller %proteins% transcribed from internal promoters located further downstream, and lack important domains of dystrophin. Several other genes, encoding evolutionarily related %proteins%, have been identified. To study the evolution of the DMD gene and the significance of its various products, we have searched for genes encoding dystrophin-like %proteins% in sea urchin and in Drosophila. We previously reported on the characterization of a sea urchin gene encoding a %protein% which is an evolutionary homologue of Dp116, one of the small products of the mammalian DMD gene, and on the partial sequencing of a large product of the same gene. Here we describe the full-length product which shows strong structural similarity and sequence identity to human dystrophin and utrophin. We also describe a Drosophila gene closely related to the human dystrophin gene. Like the human gene, the Drosophila gene encodes at least three isoforms of full length dystrophin-like %proteins% (dmDLP1, dmDLP2 and dmDLP3,), regulated by different promoters located at the 5prime end of the gene, and a smaller product regulated by an internal promoter (dmDp186). As in mammals, dmDp186 and the dmDLPs share the same C-terminal and %cysteine%-rich domains which are very similar to the corresponding domains in human dystrophin and utrophin. In addition, dmDp186 contains four of the spectrin-like repeats of the dmDLPs and a unique N-terminal region of 512 amino acids encoded by a single exon. The full length products and the small product have distinct patterns of expression. Thus, the complex structure of the dystrophin gene, encoding several large dystrophin-like isoforms and smaller truncated products with different patterns of expression, existed before the divergence between the protostomes and deuterostomes. The conservation of this gene structure in such distantly related organisms, points to important distinct functions of the multiple products. (c) 2001 Elsevier Science B.V.

2/7/13 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

12078195 EMBASE No: 2003175994
Type II and type IX collagen transcript isoforms are expressed during mouse testis development
McClive P.J.; Sinclair A.H.
P.J. McClive, Department of Paediatrics, University of Melbourne, Royal Children's Hospital, Melbourne, Vic. 3052 Australia
AUTHOR EMAIL: mcclivep@cryptic.rch.unimelb.edu.au
Biology of Reproduction (BIOL. REPROD.) (United States) 01 MAY 2003, 68/5 (1742-1747)
CODEN: BIREB ISSN: 0006-3363
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 45

Mutations in the transcription factor SOX9 give rise to campomelic dysplasia, a syndrome characterized by skeletal abnormalities and XY sex reversal. Sox9 is expressed at sites of chondrogenesis and in the developing testis, and, thus, it plays a role in two overtly different pathways of differentiation. Previous studies have identified the gene for type II collagen, Col2a1, as a target of Sox9 in mouse chondrocytes and implicated Col9a3 as a Sox9 target in testis. Using differential expression analysis combined with reverse transcription-polymerase chain reaction and whole-mount in situ hybridization, we have identified nonchondrocytic collagen transcript isoforms that are expressed in the early male mouse gonad. Male-specific, gonadal expression of nonchondrocytic Col2a1 was first seen at 11.5 days postcoitum (dpc) and was undetectable by 13.5 dpc. This was accompanied by increasing expression of nonchondrocytic Col9a1, Col9a2, and Col9a3, first detected at 11.5 dpc. Expression was analyzed in testes that had been depleted of germ cells by the cytotoxic drug busulfan. These studies showed Col9a3 and Col2a1 to be expressed in Sertoli cells within the developing testis cords. Nonchondrocytic type II collagen contains a %cysteine%-rich domain that has been shown to bind members of the transforming growth factor beta superfamily of signaling molecules. Thus, this interaction may play a role in the %morphogenesis% and differentiation of the testis.

2/7/14 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

12069386 EMBASE No: 2003175276
Bone %morphogenetic% %proteins%, their antagonists, and the %skeleton%
Canalis E.; Economides A.N.; Gazzerro E.
Dr. E. Canalis, Department of Research, S. Francis Hosp. and Medical Center, 114 Woodland Street, Hartford, CT 06105-1299 United States
AUTHOR EMAIL: ecanalis@stfranciscare.org
Endocrine Reviews (ENDOCR. REV.) (United States) 01 APR 2003, 24/2 (218-235)
CODEN: ERVID ISSN: 0163-769X
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 243

Skeletal homeostasis is determined by systemic hormones and local factors. Bone %morphogenetic% %proteins% (BMP) are unique because they induce the differentiation of mesenchymal cells toward cells of the osteoblastic lineage and also enhance the differentiated function of the osteoblast. However, the activity of BMPs needs to be tempered by intracellular and extracellular antagonists. BMPs bind to specific receptors and signal by phosphorylating the cytoplasmic %proteins% mothers against decapentaplegic (Smad) 1 and 5, which form heterodimers with Smad 4, and after nuclear translocation regulate transcription. BMP antagonists can be categorized as pseudoreceptors that compete with signaling receptors, inhibitory Smads that block signaling, intracellular binding %proteins% that bind Smad 1 and 5, and factors that induce ubiquitination and proteolysis of signaling Smads. In addition, a large number of extracellular %proteins% that bind BMPs and prevent their binding to signaling receptors have emerged. They are the components of the Spemann organizer, noggin, chordin, and follistatin, members of the Dan/Cerberus family, and twisted gastrulation. The antagonists tend to be specific for BMPs and are regulated by BMPs, indicating the existence and need of local feedback mechanisms to temper BMP cellular activities.

2/7/15 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0388895 DBR Accession No.: 2006-02391 PATENT
Novel %osteogenic% %protein% comprising %polypeptide% chain capable of inducing endochondral bone formation in association with matrix when

implanted in mammal, useful for cartilage repair for treatment of osteoarthritis - involving vector-mediated gene transfer and expression in mammal progenitor cell for induced endochondral bone formation

AUTHOR: OPPERMANN H; OZKAYNAK E; KUBERASAMPATH T; RUEGER D C; PANICALI L

PATENT ASSIGNEE: STRYKER CORP 2005

PATENT NUMBER: US 20050255141 PATENT DATE: 20051117 WPI ACCESSION NO.: 2006-016983 (200602)

PRIORITY APPLIC. NO.: US 51568 APPLIC. DATE: 20050204

NATIONAL APPLIC. NO.: US 51568 APPLIC. DATE: 20050204

LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - An %osteogenic% %protein% comprising a %polypeptide% chain capable of inducing endochondral bone formation in association with a matrix when implanted in a mammal, where the %polypeptide% chain has %cysteine% residues in the same relative positions as the %cysteine% %skeleton% sequence having a fully defined 97 amino acids (SEQ ID No. 31) sequence given in specification, or its allelic variant or mutant %protein%, is new. DETAILED DESCRIPTION - An %osteogenic% %protein% (I) comprising a %polypeptide% chain capable of inducing endochondral bone formation in association with a matrix when implanted in a mammal, where the %polypeptide% chain has %cysteine% residues in the same relative positions as the %cysteine% %skeleton% sequence having a fully defined 97 amino acids (SEQ ID No. 31) sequence given in specification or the %cysteine% %skeleton% sequence having the amino acid residues 335-431 encoded by a fully defined 1822 base pairs (SEQ ID No. 1) sequence given in specification or its allelic variant or mutant %protein% that has an altered conserved C-terminal %cysteine% %skeleton%, where the %protein% or its allelic variant or mutant %protein% is capable of forming a dimeric species having a conformation capable of inducing bone formation in a mammal, where the %polypeptide% is encoded by a nucleic acid that hybridizes selectively to a nucleic acid encoding amino acid residues 335-431 of (SEQ ID No. 1) in 40% formamide, 5 x SSPE, 5 x Denhardt's solution, and 0.1% sodium dodecyl sulfate (SDS) at 37 degreesC overnight, and washing in 0.1 x SSPE, 0.1% SDS at 50 degreesC. An INDEPENDENT CLAIM is also included for an %osteogenic% device (II) for implantation in a mammal, comprises a biocompatible, in vivo biodegradable matrix defining pores of a dimension sufficient to permit influx, differentiation, and proliferation of migratory progenitor cells from the body of the mammal, and (I). BIOTECHNOLOGY - Preferred %Osteogenic% %Protein%: (I) is dimeric. The %polypeptide% is glycosylated or unglycosylated. Preferred %Osteogenic% Device: In (II), the matrix comprises collagen and a material chosen from polymers comprising lactic acid monomer units, polymers comprising glycolic acid monomer units, bone, hydroxyapatite, calcium phosphate, muscle and tissue. ACTIVITY - Osteopathic; Antiarthritic. No biological data given. MECHANISM OF ACTION - Bone formation inducer (claimed). USE - (II) is useful for inducing endochondral bone formation in a mammal or inducing local cartilage formation in a mammal, which involves implanting (II) in the mammal at a locus accessible to migratory progenitor cells of the mammal (claimed). (I) is useful in cartilage repair for the treatment of osteoarthritis.(151 pages)

2/7/16 (Item 2 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.

0380954 DBR Accession No.: 2005-26660 PATENT

Promoting dendrite outgrowth, useful for treating CNS disorder, comprises contacting the neuron with a composition comprising a %morphogen% - dendrite cell outgrowth promotion using recombinant bone %morphogenetic% %protein% for use in disease therapy

AUTHOR: RUEGER D C; SAMPATH K T; SMART J E; OPPERMANN H; OZKAYNAK E; COHEN C M; HIGGINS D

PATENT ASSIGNEE: CURIS INC; UNIV NEW YORK STATE RES FOUND 2005

PATENT NUMBER: US 6949505 PATENT DATE: 20050927 WPI ACCESSION NO.: 2005-646750 (200566)

PRIORITY APPLIC. NO.: US 292782 APPLIC. DATE: 19940818

NATIONAL APPLIC. NO.: US 292782 APPLIC. DATE: 19940818

LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - Promoting dendrite outgrowth by a neuron comprising contacting the neuron with a composition comprising a %morphogen%, is new. DETAILED DESCRIPTION - Promoting dendrite outgrowth by a neuron comprising contacting the neuron with a composition containing a %morphogen%, where the %morphogen% comprises a dimeric %protein% having an amino acid sequence selected from: (a) a conserved C-terminal seven-%cysteine% %skeleton% at least 60 % or 70 % identical homologous to the residues 38-139 of a sequence of 139 amino acids (SEQ ID NO: 5); (b) generic sequence 3 or 4 comprising 97 or 102 amino acids (SEQ ID NOS: 3 or 4), respectively; (c) generic sequence 5 or 6 comprising 139 amino acids each (SEQ ID NOS: 30 or 31); or (d) generic sequence OPX comprising 102 amino acids (SEQ ID NO: 29), where the %morphogen% promotes dendrite outgrowth in the neuron. BIOTECHNOLOGY - Preferred Method: The %morphogen% comprises residues 38-139 of SEQ ID NO: 5 or the amino acid sequence of SEQ ID NO: 5. The %morphogen% comprises residues 38-139 of SEQ ID NO: 6 or the amino acid sequence of SEQ ID NO: 6. The %morphogen% is a CBMP2 %polypeptide%, which comprises the sequence of 101 amino acids (SEQ ID NOS: 9 or 10). The %morphogen% is a BMP-6 %polypeptide%, which comprises the sequence of 102 amino acids (SEQ ID NO: 28). The %morphogen% is a 60A %polypeptide%, which comprises the sequence of SEQ ID NO: 24. The composition includes NGF. The neurons are sympathetic neurons. The %morphogen% is human OP-1, mouse OP-1, human OP-2, mouse OP-2, BMP5, BMP6, Vgr-1, 60A, BMP2A, BMP-2B, DPP, Vg1, GDF-1, or BMP3. ACTIVITY - CNS-Gen; Neuroprotective; Nootropic; Antiparkinsonian; Antidiabetic. No biological data given. MECHANISM OF ACTION - Gene Therapy. USE - The methods and composition comprising a %morphogen% are useful for promoting dendrite outgrowth by a neuron and for treating CNS disorder, e.g. Alzheimer's disease, Parkinson's disease, dementia, or diabetic neuropathy. ADMINISTRATION - Dosage is 2-20 micrograms/kg by parenteral, e.g. intravenous, subcutaneous, intramuscular, intraorbital, ophthalmic, intraventricular , intracranial, intracapsular, intraspinal, intracisternal, intraperitoneal, buccal, rectal, vaginal, or intranasal means. EXAMPLE - Suspensions of neurons dissociated from the superior cervical ganglia of Sprague-Dawley rat fetuses (19-21 day) or rat pups (1-3 day postnatal) were prepared. Neurons were plated at low density (10 cells/mm2) onto poly-D-lysine coated (100 micrograms/ml) cover slips and maintained in a serum-free medium containing NGF (100 ng/ml Cytosine-beta-D-furanoside (1 muM) was added to the medium of all cultures for 48 hours on the second day. Ganglia from 15-day embryos were grown in explant culture for 18 hours in the presence of 3H-(methyl)-thymidine (0.3 microcoulombi/ml, ICN) before being dissociated. NT3 (50 ng/ml) was added to the NGF-containing medium during the period of explant culture and the next 4 days in vitro. As in cultures of sympathetic neurons, exposure to NGF, OP-1 or both was initiated after the elimination of non-neuronal cells. Cellular morphology was routinely assessed. Only neurons whose cell bodies were at least 150 microns from their nearest neighbor were injected. Mature human recombinant OP-1 was isolated from medium conditioned by transfected Chinese hamster ovary cells. Under control conditions, sympathetic neurons typically extended a single process during the first 24-48 hours in vitro. This process has the cytoskeletal and ultrastructural characteristics of an axon. The axon continued to elongate during the next few weeks and generate an elaborate plexus. The basic morphology of the cells, however, remained essentially unchanged, with 80 % of the neurons still being unipolar after 1 month in vitro. Most of the remainder had either 2 axons (13 % of the cells) or an axon and a short dendrite (7 %). Thus, the mean number of processes at this time was 1.13 plus minus 0.06 axons/cells and 0.07 plus minus 0.04 dendrites/cell. Exposure to OP-1 caused sympathetic neurons to form additional processes. This response was relatively slow with 10 only 42 % of the cells forming a second process within 24 hours. However, virtually all cells (94 %) had begun to respond to maximal concentrations of OP-1 within 3 days. The processes that formed in the presence of OP-1 had the appearance of dendrites in that they were broad-based (up to 15 microns diameter), exhibited a distinct taper, and branched in a "Y"-shaped pattern, with daughter processes being distinctly smaller than the parent process. Dendrites were much thicker than sympathetic axons and, unlike axons, they ended locally,

usually extending less than 300 microns from the soma. The mean number of dendrites/cell continued to increase during a 4-week exposure to OP-1 with most of the change occurring during the first 10 days of treatment. After 4 weeks, OP-l-treated neurons had a mean of 7.3 plus minus 0.3 dendrites/cell, representing a 100-fold increase over control cells. During this time, the size of the dendritic arbor also increased with cells progressing from simple cells to a more complicated morphology.(68 pages)

2/7/17 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0367663 DBR Accession No.: 2005-13369 PATENT
Preserving motor function in a mammal with symptoms of or at risk of amyotrophic lateral sclerosis or a spinal cord injury comprises administering to the mammal a %morphogen% - motor function preservation treatment for motor neuron injury and neuropathy therapy or gene therapy
AUTHOR: RUEGER D C; SAMPATH K T; OPPERMANN H; PANG R H L; COHEN C M
PATENT ASSIGNEE: RUEGER D C; SAMPATH K T; OPPERMANN H; PANG R H L; COHEN C M 2005
PATENT NUMBER: US 20050065083 PATENT DATE: 20050324 WPI ACCESSION NO.: 2005-241295 (200525)
PRIORITY APPLIC. NO.: US 806852 APPLIC. DATE: 20040323
NATIONAL APPLIC. NO.: US 806852 APPLIC. DATE: 20040323
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - Preserving motor function in a mammal with symptoms of or at risk of amyotrophic lateral sclerosis or a spinal cord injury comprises administering to the mammal a %morphogen%, e.g. human OP-1, mouse OP-1, human OP-2, mouse OP-2,60A, GDF-1, BMP2A, BMP2B, DPP, Vgl, Vgr-1, BMP3, BMP5, or BMP6. DETAILED DESCRIPTION - Preserving motor function in a mammal with symptoms of or at risk of amyotrophic lateral sclerosis or a spinal cord injury comprises administering to the mammal a %morphogen%, e.g. human OP-1, mouse OP-1, human OP-2, mouse OP-2,60A, GDF-1, BMP2A, BMP2B, DPP, Vgl, Vgr-1, BMP3, BMP5, or BMP6, where %morphogen% comprises a dimeric %protein% having an ammo acid sequence with: (i) at least 70% homology with the C-terminal seven-%cysteine% %skeleton% of human OP-1, residues 330-431 of a sequence of 431 amino acids (SEQ ID NO: 2); (ii) having greater than 60% amino acid sequence identity with the C-terminal seven-%cysteine% %skeleton% of human OP-1; (iii) defined by Generic Sequences 7-10, respectively comprising a sequence of 97, 102, 97, or 102 amino acids (SEQ ID NOS: 4-7); or (iv) defined by OPX, comprising a sequence of 102 amino acids (SEQ ID NO: 3), and stimulates production of an N-CAM or L1 isoform by an NG108-15 cell in vitro, where motor function is preserved in the mammal. ACTIVITY - CNS-Gen; Muscular-Gen; Neuroprotective; Vulnerary. No biological data given. MECHANISM OF ACTION - Gene Therapy. USE - The method and %morphogen% are useful for preserving motor function in a mammal with symptoms of or at risk of amyotrophic lateral sclerosis or a spinal cord injury. The methods and composition are useful for treating motor neuron injury and neuropathy like amyotrophic lateral sclerosis, spinal cord injury or multiple sclerosis. ADMINISTRATION - Dosage is 0.00001-1000 mg/kg, preferably 0.001-10 mg/kg, by topical, oral, or parenteral including intravenous, subcutaneous, intramolecular, ophthalmic, intraperitoneal, intramuscular, buccal, rectal, vaginal, intraorbital, intracerebral, intracranial, intraspinal, intraventricular, intrathecal, intracisternal, intracapsular, intranasal, or by aerosol means. (55 pages)

2/7/18 (Item 4 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0320277 DBR Accession No.: 2003-21417 PATENT
%Osteogenic% device useful for inducing endochondral bone formation in mammals, comprises ceramic or biodegradable non-collagen polymer matrix containing substantially pure natural-sourced mammalian %osteogenic% %protein% - apparatus for %protein% delivery and disease therapy
AUTHOR: OPPERMANN H; OZKAYNAK E; KUBERASAMPATH T; RUEGER D C; PANG R H L
PATENT ASSIGNEE: STRYKER CORP 2003
PATENT NUMBER: US 6551995 PATENT DATE: 20030422 WPI ACCESSION NO.: 2003-575998 (200354)
PRIORITY APPLIC. NO.: US 148925 APPLIC. DATE: 19980904
NATIONAL APPLIC. NO.: US 148925 APPLIC. DATE: 19980904
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - An %osteogenic% device (I) for implantation in a mammal, comprising a ceramic or biodegradable non-collagen polymer matrix (II) defining pores of a dimension sufficient to permit influx, differentiation and proliferation of migratory progenitor cells from the body of mammal, and a substantially pure %osteogenic% %protein% competent to induce endochondral bone formation when disposed in (II) and implanted in mammal, is new. BIOTECHNOLOGY - Preferred Device: The matrix comprises a shape-retaining solid which is in the form of a sheet, an aggregate of particles, a rod, a bead, or macroscopic shape. The %osteogenic% %protein% comprises a pair of glycosylated or unglycosylated %polypeptide% chains which form a dimer. The %osteogenic% %protein% comprises an amino acid sequence selected from: (a) Ala-Cys-Cys-Val-Pro-Thr-Glu-Leu-Ser-Ala-Ile-Ser-Met-Leu-Tyr-Leu-Asp-Glu ; (b) Asn-Glu-Lys; (c) Val-Pro-Lys-Pro; and (d) Ala-Pro-Thr. Each of the %polypeptide% chains is encoded by a DNA, one strand of which hybridizes selectively to a DNA sequence comprising 314 bp fully defined in the specification, where the hybridization is preferably performed in 5 x SSPE, 10 x Denhardt's mix, and 0.5% sodium dodecylsulfate (SDS) at 50 degreesC. Each of the %polypeptide% chains of the pair has at least 96 amino acids and less than 200 amino acids, and has a molecular weight of 14-16 kDa in an unglycosylated form or a molecular of 16-18 kDa in a glycosylated form as determined by polyacrylamide gel electrophoresis under reducing conditions. Each of the %polypeptide% chains comprises at least 6 %cysteine% residues in the same relative positions as the 6 %cysteine% %skeleton% sequence of amino acid residues 335-431 of a sequence comprising 431 amino acids fully defined in the specification. Each of the %polypeptide% chains comprises at least 7 %cysteine% residues in the same relative positions as the seven %cysteine% %skeleton% sequence of amino acid residues 330-431 of a sequence comprising 431 amino acids fully defined in the specification. USE - (I) is useful for producing endochondral bone formation in mammals, for bone and cartilage repair, for inducing the full developmental cascade of endochondral bone formation including vascularization, mineralization and bone marrow differentiation at the locus of an implant when implanted in a mammalian body. (I) is useful for bone formation in various orthopedic, periodontal and reconstructive procedures. ADVANTAGE - A number of bone derived %proteins% have been described which may induce endochondral bone formation (e.g. see Sampath et al. (1987) Proc. Natl. Acad. Sci. USA 84:7109-7113 and PCT/087/01537). The applicants provide novel %osteogenic% %polypeptides% (and also their encoding DNAs) which improve the effectiveness of the implant.(127 pages)

2/7/19 (Item 5 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0254033 DBR Accession No.: 2000-08523 PATENT
Novel TGF-beta superfamily mutant chimeric %protein%, useful for inducing tissue %morphogenesis% in e.g. bone, comprises a dimer consisting of one monomer containing domains from two family members - recombinant transforming growth factor-beta production and purification via Escherichia coli vector plasmid-mediated gene transfer and expression in host cell for therapy
AUTHOR: Oppermann H; Tai M S; McCartney J
CORPORATE SOURCE: Kalamazoo, MI, USA.
PATENT ASSIGNEE: Stryker 2000
PATENT NUMBER: WO 200020591 PATENT DATE: 20000413 WPI ACCESSION NO.:

2000-303776 (2026)
PRIORITY APPLIC. NO.: US 374936 APPLIC. DATE: 19990816
NATIONAL APPLIC. NO.: WO 99US23370 APPLIC. DATE: 19991007
LANGUAGE: English
ABSTRACT: A transforming growth factor (TFG)-beta superfamily chimeric %protein% (I) derived from at least 2 different members of the superfamily which consists of a dimer with one monomer that contains a finger 2 domain derived from a first family member and a conserved C-terminal %cysteine% %skeleton% , and a finger 1 domain and heel domain, both derived from a second family member, is new. Also claimed are: a DNA sequence encoding the monomer of (I); and a method for determining the epitope recognized by an antibody that binds a first TGF-beat superfamily chimeric %protein%, but does not bind a second. (I) may be useful for inducing tissue %morphogenesis% (i.e. molecules capable of tissue repair and regeneration and/or inhibiting inflammation) in bone, non-mineralized skeletal tissue, dental tissue, connective tissue, brain, liver and nerve, and for inducing the proliferation and differentiation of uncommitted progenitor cells in a tissue-specific manner to support new tissue formation. In an example, an Escherichia coli expression vector plasmid was used to construct (I) and it was expressed in a host cell and isolated using standard techniques. (146pp)

2/7/20 (Item 6 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0247844 DBR Accession No.: 2000-02334 PATENT
Screening assay useful for identifying compounds which can act to modulate expression of a %morphogen% in a mammalian cell - drug screening
AUTHOR: Smart J E; Oppermann H; Ozkaynak E; Kuberasampath T; Rueger D C ; Pang R H L; Cohen C M
CORPORATE SOURCE: Hopkinton, MA, USA.
PATENT ASSIGNEE: Creative-Biomol. 1999
PATENT NUMBER: US 5994131 PATENT DATE: 19991130 WPI ACCESSION NO.: 2000-038265 (2003)
PRIORITY APPLIC. NO.: US 912088 APPLIC. DATE: 19970815
NATIONAL APPLIC. NO.: US 912088 APPLIC. DATE: 19970815
LANGUAGE: English
ABSTRACT: Altering expression of a %morphogen% in a mammalian cell with a compound identified by a screening assay is claimed. Also claimed is a method for altering the expression of a %morphogen% in a mammal cell, which involves: (1) providing a compound that modulates %morphogen% expression in epithelium cells identified in an assay for bone formation; and (2) contacting a mammal cell with the compound to alter %morphogen% expression in that cell. (1) involves: incubating the compound with epithelium cells expressing a %protein% which induces endochondral bone formation in an in vivo assay (a %protein% with at least 70% homology with the C-terminal 7 %cysteine% domain of human OP-1 %morphogenic% %protein% of the transforming growth factor superfamily, a %protein% of 102 amino acids which provides a %cysteine% %skeleton% or where disulfide bonds can form containing a certain critical amino acid influencing the tertiary structure of the %protein% , or a %protein% %morphogen% e.g. mouse or human OP-1 or OP-2); measuring a test amount of the %protein% expressed by epithelium cells in the presence of the test compound; and comparing this amount to the amount of %protein% expressed in the absence of the test compound. (48pp)
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26jun06 09:12:18 User219511 Session D648.4
$2.36 0.693 DialUnits File155
$2.20 10 Type(s) in Format 7
$2.20 10 Types
$4.56 Estimated cost File155
$2.38 0.403 DialUnits File5
$2.05 1 Type(s) in Format 7
$2.05 1 Types
$4.43 Estimated cost File5
$1.54 0.175 DialUnits File71
$2.10 1 Type(s) in Format 7
$2.10 1 Types
$3.64 Estimated cost File71
$5.01 0.448 DialUnits File73
$6.20 2 Type(s) in Format 7
$6.20 2 Types
$11.21 Estimated cost File73
$2.40 0.108 DialUnits File357
$23.76 6 Type(s) in Format 7
$23.76 6 Types
$26.16 Estimated cost File357
OneSearch, 5 files, 1.826 DialUnits FileOS
$0.53 TELNET
$50.53 Estimated cost this search
$55.74 Estimated total session cost 3.534 DialUnits
File 411:DIALINDEX(R)

DIALINDEX(R)
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*** DIALINDEX search results display in an abbreviated ***
*** format unless you enter the SET DETAIL ON command. ***
You have 25 files in your file list.
(To see banners, use SHOW FILES command)
? s (morphogen? or osteogen?) and (protein? or polypeptide?) and (cysteine? or cystine?)

Your SELECT statement is:
s (morphogen? or osteogen?) and (protein? or polypeptide?) and (cysteine? or cystine?)

Items	File
259	5: Biosis Previews(R)_1969-2006/Jun W3
12	8: Ei Compendex(R)_1970-2006/Jun W3
137	24: CSA Life Sciences Abstracts_1966-2006/May
543	34: SciSearch(R) Cited Ref Sci_1990-2006/Jun W3
1	65: Inside Conferences_1993-2006/Jun 23
226	71: ELSEVIER BIOBASE_1994-2006/Jun W4
313	73: EMBASE_1974-2006/Jun 26
46	94: JICST-EPlus_1985-2006/Mar W4
16	98: General Sci Abs_1984-2005/Jan
14	135: NewsRx Weekly Reports_1995-2006/Jun W3
2	136: BioEngineering Abstracts_1966-2006/May
14	143: Biol. & Agric. Index_1983-2006/May
64	144: Pascal_1973-2006/Jun W1
379	155: MEDLINE(R)_1951-2006/Jun 20
5	172: EMBASE Alert_2006/Jun 26
25	266: FEDRIP_2005/Dec
3	315: ChemEng & Biotec Abs_1970-2006/May
59	357: Derwent Biotech Res._1982-2006/Jun W3
3	358: Current BioTech Abs_1983-2006/Jan
1	369: New Scientist_1994-2006/Jun W3
9	370: Science_1996-1999/Jul W3
80	399: CA SEARCH(R)_1967-2006/UD=14426
11	434: SciSearch(R) Cited Ref Sci_1974-1989/Dec

23 files have one or more items; file list includes 25 files.

? bye
26jun06 09:13:08 User219511 Session D648.5
$5.39 2.033 DialUnits File411
$5.39 Estimated cost File411
$0.26 TELNET
$5.65 Estimated cost this search
$61.39 Estimated total session cost 5.567 DialUnits
Logoff: level 05.12.03 D 09:13:08

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	"20050054825"	US-PGPUB	OR	OFF	2006/06/22 17:20
L2	5925	(BMP or ostegenic or GDF) and bone	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/06/22 17:20
L3	131	cysteine same skeleton	USPAT	OR	OFF	2006/06/22 17:20
L4	91	2 and 3	USPAT	OR	OFF	2006/06/22 17:21
L5	131	(oppermann.in. or kuberasampath.in. or rueger.in. or ozkaynak.in.) and bone	US-PGPUB; USPAT	OR	OFF	2006/06/22 17:22
L6	96	(oppermann.in. or kuberasampath.in. or rueger.in. or ozkaynak.in.) and bone	USPAT	OR	OFF	2006/06/22 17:22